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Trodelvy® (sacituzumab govitecan-hziy) Neutropenia and Growth Factor Support: Real-World Studies of SG in mBC

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hzyi [SG]), neutropenia, and use of growth factors in real-world metastatic breast cancer (mBC) studies: triple-negative breast cancer (TNBC) and hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) breast cancer.

This document summarizes data for SG monotherapy from global real-world studies in patients with mBC.

Gilead continually assesses safety data from all sources for unidentified drug reactions and updates the product label information accordingly to reflect the safety profile of SG. Because case reports of potential adverse reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish causal relationship to drug exposure. For this reason, Gilead does not provide information from post-marketing spontaneous reports.

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The full indication, important safety information, and boxed warnings for neutropenia and diarrhea are available at: www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.

Summary

Relevant Product Labeling[1]

SG can cause severe, life-threatening, or fatal neutropenia as early as the first cycle of treatment. Neutropenia occurred in 64% of patients treated with SG. Grade 3-4 neutropenia occurred in 49% of patients. Febrile neutropenia occurred in 6% of patients. The median time to first onset of neutropenia (including febrile neutropenia) was 16 days (range: 1–435 days). Neutropenia occurred earlier in patients with reduced UGT1A1 activity. Neutropenic colitis occurred in 1.4% of patients.

Primary prophylaxis with G-CSF is recommended starting in the first cycle of treatment in all patients at increased risk of febrile neutropenia, including older patients, patients with previous neutropenia, poor performance status, organ dysfunction, or multiple comorbidities.

Monitor ANC during treatment. Withhold SG for ANC below 1500/mm^3 on Day 1 of any cycle or below 1000/mm^3 on Day 8 of any cycle. Withhold SG for neutropenic fever. Dose modifications may be required due to neutropenia. Treat neutropenia with G-CSF and administer prophylaxis in subsequent cycles as clinically indicated or indicated in Table 2 of the Prescribing Information.

Incidence of Neutropenia and Use of Growth Factors: Real-World Data[2-9]

This summary presents neutropenia rates and growth factor use (as primary or secondary prophylaxis) during SG treatment in clinical practice, based on global real-world mBC studies.

Incidence of neutropenia and growth factor use on clinical outcomes, duration of SG treatment, and the occurrence of SG dose modifications is presented. In addition, the effect of the initial SG dose on neutropenia risk is examined.

Real-World Studies of SG in mBC

Incidence and Management of Neutropenia

Neutropenia prevalence and G-CSF use in mTNBC[2]

A US, retrospective, observational cohort study assessed SG data from the Flatiron Health database to evaluate 381 patients with mTNBC who had received SG in the 2L+ setting. The median (IQR) age of patients was 61 y (52–69); 61% and 18% identified as White and as Black/African American, respectively. Patients received a median (IQR) of 2 (1–3) prior LoT in the metastatic setting. In the 2L setting, 31% (n=118) of patients received SG and 69% (n=263) of patients in the 3L+ setting.

Patients received a median (IQR) of 12 (5–21) SG doses. Of the patients with dosing data (n=308), 44% (n=137) had a dose reduction. Treatment duration is summarized in Table 1.

Table 1. SG Treatment Duration[2]

	All Patients (n=381)	SG in 2L (n=118)	SG in 3L+ (n=263)
Duration, median (IQR), mo	4 (1.9–7.6)	4.2 (1.6–8.1)	4 (2.1–7.4)

Safety

Incidence of Grade 2 and ≥3 neutropenia was 25% (n=94) and 27% (n=101), respectively. During SG treatment, 225 patients (59%) received G-CSF; 117 patients received G-CSF as prophylaxis (primary prophylaxis [n=77], secondary prophylaxis [n=36], both [n=4]). Grade ≥3 neutropenia occurred in 12 patients (10%) after any G-CSF prophylaxis and in 3 patients (4%) receiving primary prophylaxis. Median time from the start of SG treatment to first onset of Grade ≥3 neutropenia was 48 d; see Table 2 for results stratified by G-CSF use.

Table 2. Incidence and Time to First Onset of Grade ≥3 Neutropenia[2]

Grade ≥3 Neutropenia	G-CSF Use			
	Did Not Receive (n=156)	Therapeutic G-CSF[a] (n=24)	Secondary prophylaxis (n=36)	Primary prophylaxis (n=77)
n (%)	21 (13)	8 (33)	7 (19)	3 (4)
Time to Onset, median (IQR), d	8 (8–22)	NA	42 (36–56)	48 (36–322)

Abbreviation: NA=not applicable

[a]Administered on or after neutropenia onset and before its resolution or SG treatment end.

Neutropenia prevalence and G-CSF use in mBC[3]

A single-center, retrospective cohort, mBC study (N=74) examined electronic health records for clinical features, prior treatments, safety outcomes, and use of G-CSF in patients who had received SG.

The median age (range) of patients was 56.5 y (28.4–81.1). Patients with mTNBC had received a median (range) of 2 (0–5) previous chemotherapy regimens; patients with HR+/HER2- mBC had received a median (range) of 8 (2–14) prior LoT, including 4 (0–8) lines of chemotherapy. The median duration (range) of SG therapy was 4.4 mo (0.26–39.8) for mTNBC patients and 1.9 mo (0.26–15.6) for those with HR+/HER2- mBC.

Rates of any-grade and Grade 3 neutropenia are shown in Table 3. A total of eight patients (10.8%) were hospitalized for SG-related neutropenia with median stay (range) of 3.5 d (1–10). About half of all dose delays were due to neutropenia.

Table 3. Incidence of Neutropenia[3]

Outcomes, n (%)	All Patients (N=74[a])	mTNBC (n=45)	HR+/HER2- mBC (n=27)
Any-grade neutropenia	60 (81.1)	37 (82.2)	21 (77.8)
Grade 3 neutropenia	39 (52.7)	25 (55.6)	12 (44.4)
Neutropenic fever	5 (6.8)	4 (8.9)	NR
Dose delays	-	18 (40)	8 (29.6)
Due to neutropenia	-	7 (15.6)	4 (14.8)
Dose reductions	-	21 (46.7)	18 (66.7)
Due to neutropenia	-	7 (15.6)	4 (14.8)

NR=not reported

[a]Two patients (2.7%) with mixed receptor expression were classified as HR+/HER2+ mBC.

Most patients (n=64, 86.5%) received G-CSF during SG treatment (Table 4). Rates of primary and secondary prophylaxis varied for patients with mTNBC and HR+/HER2- mBC.

Table 4. Incidence of G-CSF use[3]

	Received filgrastim	Received peg-filgrastim	Primary prophylaxis	Secondary prophylaxis
G-CSF use, n (%)	62 (83.8)	7 (9.5)	34 (45.9)	24 (32.4)
mTNBC, %	-	-	37.8	40
HR+/HER2- mBC, %	-	-	55.6	22.2

Neutropenia Prevalence, G-CSF Use and Impact on DOT

Two US studies have evaluated SG data from the IntegraConnect PrecisionQ database, specifically examining the use of G-CSF and its effect on DOT.[4,5]

Neutropenia prevalence, G-CSF use and impact on DOT in patients with cancer[4]

Data was assessed for neutropenia prevalence, G-CSF use and impact on DOT in 447 patients (cancer type was not reported). Patients were on average (median) 58.5 y (60); 69% and 15% identified as White/Caucasian and as Black/African American, respectively. A total of 98% of SG-treated patients developed neutropenia; of these, 61% received G-CSF.

Median DOT was 119.5 d for patients with ≥12 mo follow-up (n=330); see Table 5 for the median DOT in patients who did or did not receive G-CSF.

Table 5. DOT and G-CSF use[4]

G-CSF Use	Patients (n)	DOT, median (range), d	*P*-value
Received	204	147 (7–942)	<0.001
Did not receive	126	97 (1–1013)	

G-CSF use and impact on SG DOT in mTNBC[5]

Data was stratified by G-CSF use and assessed for DOT with SG in patients with mTNBC (N=337). The median (IQR) age at first treatment was 58.3 y (49–67); 65%, 17%, and 2% identified as White, Black/African American, and Asian, respectively. The median (IQR) time from initial breast cancer diagnosis to the first SG use was 3.3 y (1–6). Of the patients with ECOG data, 28%, 49%, 11%, 1%, and 1% were ECOG PS 0, 1, 2, 3, and 4, respectively.

A total of 202 patients (60%) used G-CSF. For primary prophylaxis (46% of cases), 65% used long-acting, 34% short-acting, and 1% both agents. For secondary prophylaxis or treatment (54% of cases), 65% used short-acting, 35% long-acting, and 1% both. DOT was stratified by G-CSF use (Table 6).

Table 6. SG DOT Stratified by G-CSF use[5]

G-CSF Use	Received	Did not receive	Primary prophylaxis	Secondary prophylaxis/ treatment	Long-acting	Short-acting
DOT, median (IQR), d	137 (71–239)	85 (44–188)	134 (65–241)	139 (71–239)	155 (72–246)	134 (71–224)

Initial SG Dose and Risk of Neutropenia[6]

A US, retrospective, single-center cohort study, evaluated the relationship of neutropenia and different starting doses of SG (10 mg/kg [70%], 7.5 mg/kg [22%] or 5 mg/kg [8%]) in 366 patients with HER2- mBC. Patient demographics and disease characteristics, treatment patterns, safety outcomes, and G-CSF use were evaluated. To control for confounding variables, inverse probability weighting, based on propensity scores was applied.

Results showed that dose reductions were more common when patients initiated SG 10 mg/kg (42%) vs 7.5 mg/kg (16%); 66% of the reductions were due to neutropenia. Three patients discontinued treatment due to toxicity. After adjusting for age, prior LoT and prophylactic G-CSF use, patients initiating SG 10 mg/kg had a 2.8-fold higher OR of Grade 3-4 neutropenia vs those initiating SG 5 mg/kg (OR 2.77, 95% CI: 1.29–6.27, P=0.011); DOT was shorter with the 5 mg/kg dose. Age was not associated with neutropenia risk after adjusting for starting dose, prophylactic G-CSF use, and prior LoT.

There was significantly less Grade 3-4 neutropenia with prophylactic G-CSF use (OR 0.12, 95% CI: 0.07–0.18, *P*<0.001) when controlling for age, prior LoT, and starting dose. Prophylactic G-CSF was most frequently used in patients who started treatment at reduced doses, but utilization rates did not differ by age.

Impact on Efficacy Outcomes With Prophylactic G-CSF

Impact of G-CSF prophylaxis on OS and TTD[7]

The IntegraConnect PrecisionQ database in the US was used to evaluate the impact of prophylactic G-CSF use (defined as use within 8 d of SG initiation) on TTD and OS among patients with mTNBC who had received SG (N=615). Patients were excluded with a

documented neutrophil count <1500/µL. Most patients were White (67%), 41% had ECOG PS 1, and 88% did not receive prophylactic G-CSF. Median (IQR) age at SG initiation was 60 y (53–69). Age, race, and ECOG PS did not significantly differ by prophylactic G-CSF use.

At 4 mo, the cumulative incidence of neutropenia was significantly higher among those who did not receive prophylactic G-CSF (42% vs 30%, Gray's test *P*=0.002). Median TTD and OS did not significantly differ by prophylactic G-CSF use. From 0–4 mo, patients who did not receive prophylactic G-CSF vs those who received prophylactic G-CSF <8 days of SG initiation were >2 times more likely to die, HR 2.37 (95% CI: 1.22–4.59, *P*=0.011); after 4 mo, the impact of not receiving prophylactic G-CSF on OS was less (HR 1.02, 95% CI: 0.79–1.50, *P*=0.4). There was no significant difference observed in TTD in either time-interval.

Impact of primary G-CSF prophylaxis on PFS and OS[8]

The impact of G-CSF as primary prophylaxis on real-world clinical outcomes and treatment-related AEs was evaluated in a multinational cohort of patients with mTNBC who had received SG (N=303). Baseline characteristics were balanced for prior systemic treatment for early-stage disease, the number of prior LoT in the metastatic setting, comorbidities, metastatic sites, and prior episodes of FN. However, ECOG PS 0 was more frequent in the prophylaxis group (50% vs 37.1%, *P*=0.034).

Primary prophylactic G-CSF use was not associated with improved PFS or OS (Table 7).

Table 7. Impact of Primary G-CSF Prophylaxis on PFS and OS[8]

G-CSF Primary Prophylaxis	Median PFS, mo		PFS at 6 mo, %	Median OS, mo		OS at 12 mo, %
	%	*P*-value		%	*P*-value	
Received	4.2	0.2	38.5	10.9	0.95	44.9
Did Not Receive	5.1		42.1	11.6		47.1

There were no statistically significant differences in the rates of all-grade AEs between groups. There was less Grade ≥3 neutropenia in patients receiving G-CSF primary prophylaxis vs patients in the no-primary prophylaxis group (33% vs 50.7%, *P*=0.005); this was not accompanied by a reduction in FN rates (4% vs 4.4%, *P*=1). Of those patients who did not receive G-CSF primary prophylaxis, 74.4% eventually required secondary G-CSF support. Only 17.2% of patients received SG without any G-CSF support.

Impact of Primary G-CSF Prophylaxis on Neutropenia[9]

A UK, retrospective, observational, case-controlled study, of data from 13 National Health Service Trusts, evaluated the impact of G-CSF as primary prophylaxis on the incidence of neutropenic sepsis, Grade 3-4 neutropenia, and dose delays and reductions in patients with mTNBC who received SG (N=217).

The addition of primary G-CSF prophylaxis reduced both the proportion of patients who had ≥1 episode of FN and the proportion of patients who had ≥1 episode of Grade 3-4 neutropenia (Table 8). Reduction in FN and Grade 3-4 neutropenia was also observed when per cycle or dose was analyzed. More dose delays were observed in patients who received primary G-CSF prophylaxis, however, the reason for the delay was not documented in all cases.

Table 8. Impact of Primary G-CSF Prophylaxis on Neutropenia[9]

		Primary G-CSF Prophylaxis	
		Received (n=87)	Did Not Receive (n=130)
Number of cycles		519.5	976
Previous LoT, mean (median [range])		2.3 (2 [0–6])	2.4 (2 [1–7])
Number of cycles of SG, mean (median [range])		6 (4.5 [0.5–24])	7.6 (6.5 [0.5–30])
Number of doses of SG, mean (median [range])		11.9 (9 [1–42])	13.8 (12 [1–41])
Dose intensity, mean (median [range]), %		83 (83 [43–100])	85 (84 [43–100])
Neutropenia	Overall episodes, n	87	263
	Rate per dose, %	8.6	15.5
	Patients with ≥1 episode of Grade 3-4, n (%)	13 (14.9)	38 (29.2)
	Grade 3-4 episodes, n	16	68
	Rate Grade 3-4 per dose, %	1.6	4
FN	Patients with ≥1 episode, n (%)	6 (6.9)	25 (19.2)
	Episodes, n	11	29
	Rate per cycle, %	2.1	3
Dose delays	Episodes, n	114	108
	Rate per cycle, %	21.9	11.1

References

1. TRODELVY® Gilead Sciences Inc. Trodelvy (sacituzumab govitecan-hziy) for injection, for intravenous use. U.S. Prescribing Information. Foster City, CA.
2. Nanda R, Yam C, Spring L, et al. Management of neutropenia and effectiveness of sacituzumab govitecan in patients with metastatic triple-negative breast cancer treated in real-world settings in the United States [Poster P1-09-17]. presented at: San Antonio Breast Cancer Symposium (SABCS); December 10-13 2024; San Antonio, TX.
3. Fisch S, Chin J, Quintal L, et al. Single-center retrospective cohort study evaluating neutropenia and growth factor use with sacituzumab govitecan in patients with HR+/HER2- and triple negative metastatic breast cancer [Abstract P5-12-25]. Presented at: San Antonio Breast Cancer Symposium (SABCS); December 10-14, 2024 San Antonio, TX.
4. Gorantla V, Alwon E, Gart M, et al. Utilization of granulocyte colony-stimulating factor in the management of patients on sacituzumab govitecan-hziy and impact on duration of therapy [Poster PO2-18-02]. presented at: San Antonio Breast Cancer Symposium (SABCS); December 5–9 2023; San Antonio, TX.
5. Kudrik F, Gorantla V, Choski R, et al. Real-world duration of sacituzumab govitecan-hziy treatment in patients with metastatic triple-negative breast cancer [Abstract P1-07-16]. Presented at: San Antonio Breast Cancer Symposium (SABCS); December 10-14, 2024 San Antonio, TX.
6. Newman AB, Raghavendra A, Grannan E, et al. Sacituzumab govitecan dosing and neutropenia risk in patients with HER2-negative metastatic breast cancer [Poster: PS2-06-03]. Presented at: San Antonio Breast Cancer Symposium (SABCS); December 9-12, 2025; San Antonio, TX.
7. Kudrik R, Choksi R, Gorantla V, et al. Impact of overall survival on the use of prophylactic granulocyte colony-stimulating factor with sacituzumab govitecan-hziy in the treatment of triple negative metastatic breast cancer patients [Poster PS5-02-22]. Presented at: San Antonio Breast Cancer Symposium (SABCS); 09-12 December 2025; San Antonio, TX.
8. Bielčiková Z, Pieniążek M, Polakiewicz-Gilowska A, et al. Primary G-CSF prophylaxis in sacituzumab govitecan-treated mTNBC: real-world evidence from a multinational cohort [Poster PS1-05-12]. Presented at: San Antonio Breast Cancer Symposium (SABCS); 09-12 December 2025; San Antonio, TX.
9. Masters N, Langton G, Capstick C, Vafadar R. Comparing the incidence of febrile neutropenia with sacituzumab govitecan with and without primary G-CSF (granulocyte colony stimulating

factor) prophylaxis [Poster 66]. Presented at: British Oncology Pharmacy Association (BOPA) Conference; October 11-13 2024; Birmingham, UK.

Abbreviations

2L=second-line
2L+=second-line and later
3L=third-line
AE=adverse event
DOT=Duration of Therapy
ECOG PS=Eastern Cooperative Oncology Group performance status
FN=febrile neutropenia
G-CSF=granulocyte colony-stimulating factor
HR+/HER2-=hormone receptor-positive/human epidermal growth factor receptor 2-negative
LoT=lines of treatment
mBC=metastatic breast cancer
mTNBC=metastatic triple-negative breast cancer
OR=odds ratio
SG=sacituzumab govitecan-hziy
TTD= time to treatment discontinuation

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Trodelvy US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.

Follow-Up

For any additional questions, please contact Trodelvy Medical Information at:

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FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

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